

**Patent claims**

1. An osteogenic implant made of a biocompatible material, wherein the surface is at least partially covered with a polypeptide, selected from the group of transforming growth factors (TGF) and systemic hormones, or a mixture of such compounds.
2. The osteogenic implant as claimed in claim 1 with improved osteointegration properties, this implant consisting of titanium metal or a titanium-based alloy and having an at least partially roughened surface, which surface is at least partially covered, in the hydroxylated state, with a polypeptide selected from the group of transforming growth factors (TGF) and systemic hormones, or with a mixture of such compounds.
3. The osteogenic implant as claimed in claim 1, said implant containing a ceramic material, in particular an oxide ceramic.
4. The implant as claimed in claim 1 or 2, wherein it consists of a titanium/zircon alloy which, if appropriate, additionally contains niobium, tantalum or other tissue-compatible metallic additions.
5. The implant as claimed in one of claims 1 through 4, wherein it has a macro-roughness, and a micro-roughness superposed on the macro-roughness, said micro-roughness being produced by chemical etching of the surface and/or by means of electrolytic treatment, preferably by etching with an inorganic acid or a mixture of inorganic acids, preferably with hydrofluoric acid, hydrochloric acid, sulfuric acid, nitric acid or a mixture of such acids, or else by treating

the surface with hydrochloric acid, hydrogen peroxide and water in the ratio of about 1:1:5 by weight.

6. The implant as claimed in one of claims 1 through 5, wherein the transforming growth factor (TGF) is selected from the group of the (i) transforming growth factors beta (TGF- $\beta$ ) and/or the group of the (ii) bone morphogenic proteins (BMP).
7. The implant as claimed in claim 6, wherein the transforming growth factor beta (TGF- $\beta$ ) is selected from the group comprising the factors TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3, TGF- $\beta$ 4 and TGF- $\beta$ 5.
8. The implant as claimed in claim 6, wherein the bone morphogenic protein (BMP) is selected from the group comprising the proteins BMP-2 (BMP-2a), BMP-3, BMP-4 (BMP-2b), BMP-5, BMP-6, BMP-7 (OP-1), BMP-8 (OP-2), BMP-9, BMP-10, BMP-11, BMP-12, and BMP-13.
9. The implant as claimed in claim 6, wherein the bone morphogenic protein (BMP) is selected from the group comprising osteonectin, bone sialoprotein (BSP), osteopontin, osteocalcin, osteostatin, osteogenin, and osteo growth peptides (OGP).
10. The implant as claimed in claim 9, wherein the osteocalcin corresponds to the formula: H-Gly-Ala-Pro-Val-Pro-Tyr-Pro-Asp-Pro-Leu-Glu-Pro-Arg-OH.
11. The implant as claimed in claim 9, wherein the osteocalcin corresponds to the formula: H-Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-Val-OH.

12. The implant as claimed in claim 9, wherein the osteocalcin corresponds to the formula: H-Tyr-Gln-Glu-Ala-Phe-Arg-Arg-Phe-Gly-Pro-Val-OH.
13. The implant as claimed in claim 9, wherein the osteocalcin corresponds to the formula: H-Tyr-Leu-Tyr-Gln-Trp-Leu-Gly-Ala-Pro-Val-Pro-Tyr-Pro-Asp-Pro-Leu-Gla-Pro-Arg-Arg-Gla-Val-Cys-Gla-Leu-Asn-Pro-Asp-Cys-Asp-Glu-Leu-Ala-Asp-His-Ile-Gly-Phe-Gln-Gln-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-Val-OH.
14. The implant as claimed in claim 9, wherein the osteogenic growth peptide (OGP) corresponds to the formula: H-Ala-Leu-Lys-Arg-Gln-Gly-Arg-Thr-Leu-Tyr-Gly-Phe-Gly-Gly-OH.
15. The implant as claimed in one of claims 1 through 14, wherein the polypeptide, which represents a transforming growth factor (TGF) or a systemic hormone, contains at least one residue of an amino acid with a heterocyclic ring, preferably the residue of proline (Pro), hydroxyproline (Hypro), tryptophan (Try) or histidine (His).
16. The implant as claimed in one of claims 1-5, wherein the systemic hormone is the compound  $1,25-(OH)_2D_3$  or  $1\alpha,1,25(OH)_2D_3$  or  $24,25-(OH)_2D_3$ .
17. The implant as claimed in one of claims 1-16, wherein the metal surface is covered with the compound by a rate of 5%-70%, preferably 8%-50%, and in particular about 8%-20%, based on the maximum coverage of the metal surface with a monomolecular layer.

18. The implant as claimed in one of claims 1-17, wherein this implant, or at least its covered surface, is enclosed in a gas-tight and liquid-tight envelope which is filled with a gas which is inert for the implant surface, preferably with nitrogen, oxygen or a noble gas and/or at least partially with pure water, which optionally contains additives.
19. The implant as claimed in claim 18, wherein the pure water in the envelope contains a polypeptide which represents a transforming growth factor (TGF) or a systemic hormone, or a mixture of such compounds, preferably the same compound or the same mixture of compounds with which the implant surface is covered.
20. The implant as claimed in claim 19, wherein the pure water contains the polypeptide or the polypeptide mixture in a concentration in the range from 0.01  $\mu\text{mol/l}$  to 100  $\mu\text{mol/l}$ , preferably 0.1  $\mu\text{mol/l}$  to 10  $\mu\text{mol/l}$ , and preferably in a concentration of about 1  $\mu\text{mol/l}$ .
21. The implant as claimed in claim 18, wherein the pure water contains inorganic salts in the form of monovalent alkali metal cations, preferably  $\text{Na}^+$  or  $\text{K}^+$ , or a mixture of  $\text{Na}^+$  and  $\text{K}^+$ , with appropriate anions and/or divalent cations in the form of water-soluble inorganic salts, preferably  $\text{Mg}^{+2}$ ,  $\text{Ca}^{+2}$ ,  $\text{Sr}^{+2}$  and/or  $\text{Mn}^{+2}$  in the form of the chlorides, chlorates, nitrates, phosphates and/or phosphonates.
22. The implant as claimed in claim 18 or 21, wherein the pure water contains inorganic salts in a total amount of said cations and anions in each case in the range from 50 mEq/l to 250 mEq/l, preferably 100 mEq/l to 200 mEq/l, and preferably in an amount of about 150 mEq/l.

23. A process for producing an implant as claimed in one of claims 1-17, by the implant surface being shotpeened, sandblasted and/or roughened by use of plasma technology, wherein subsequently
- (i) the surface which has been roughened mechanically or by plasma technology is treated with an electrolytic or chemical etching process until a hydroxylated surface has been produced, preferably with an inorganic acid or a mixture of inorganic acids, preferably with hydrofluoric acid, hydrochloric acid, sulfuric acid, nitric acid, or a mixture of such acids, or hydrogen chloride, hydrogen peroxide and water in the ratio of about 1:1:5 by weight; and
  - (iii) the surface is at least partially covered with a polypeptide which represents an osteogenic growth peptide (OGP) or a transforming growth factor (TGF) or an osteocalcin, or with a mixture of such compounds.
24. The process as claimed in claim 23, wherein the compound is brought into contact with the hydroxylated metal surface in aqueous solution at a concentration of at least 10  $\mu\text{mol/l}$  (micromole per liter).
25. The implants produced as in claim 23 or 24.
26. The implant as claimed in one of claims 1 through 22, wherein it is a dental implant.
27. A process for introducing an osteogenic implant of at least partially cylindrical shape into a cavity of a jaw bone, wherein the bone surface, in the area of the cavity, is brought at least partially into contact with a polypeptide

selected from the group of transforming growth factors (TGF) and systemic hormones, or a mixture of such compounds.